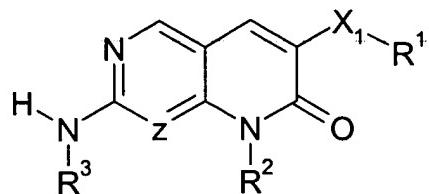


WHAT IS CLAIMED IS:

1. A compound of Formula I:



5

Formula I

or a pharmaceutically acceptable salt, hydrate or prodrug thereof,

wherein:

- 10 Z is N or CH;
 X¹ is O, NR⁴ (where R⁴ is hydrogen or alkyl), S or C=O;
 R¹ is alkyl, cycloalkyl, cycloalkylalkyl or -CH₂-alkenyl;
 R² is hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, haloalkyl,
heteroalkyl, cyanoalkyl, alkylene-C(O)-R²¹ (where R²¹ is hydrogen, alkyl, hydroxy, alkoxy,
15 amino, monoalkylamino or dialkylamino), amino, monoalkylamino, dialkylamino, acyl, or
NR²²-Y-R²³ (where Y is -C(O), -C(O)O-, -C(O)NR²⁴, S(O)₂ or S(O)₂NR²⁵; R²², R²⁴ and R²⁵
are independently hydrogen or alkyl; and R²³ is hydrogen, alkyl, cycloalkyl, cycloalkylalkyl,
heteroalkyl or optionally-substituted phenyl); and
 R³ is alkyl, haloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl,
20 cycloalkylalkyl, heteroalkylsubstituted cycloalkyl, heterosubstituted cycloalkyl, heteroalkyl,
cyanoalkyl, heterocyclyl, heterocyclalkyl, or -heterocycloamino-SO₂-R¹² (where R¹² is
haloalkyl, aryl, aryalkyl, heteroaryl or heteroaralkyl).

2. The compound of Claim 1, or a pharmaceutically-acceptable salt thereof,
25 wherein X¹ is -O-.

3. The compound of Claim 2, or a pharmaceutically-acceptable salt thereof,
wherein R¹ is alkyl or cycloalkyl.

4. The compound of Claim 3, or a pharmaceutically-acceptable salt thereof, wherein R³ is cycloalkyl, cycloalkylalkyl, heteroalkylsubstituted cycloalkyl, heterosubstituted cycloalkyl, heteroalkyl, heterocyclyl or heterocyclylalkyl.

5 5. The compound of Claim 4, or a pharmaceutically-acceptable salt thereof, wherein R³ is cycloalkyl, heteroalkylsubstituted cycloalkyl, heterosubstituted cycloalkyl, heteroalkyl or heterocyclyl.

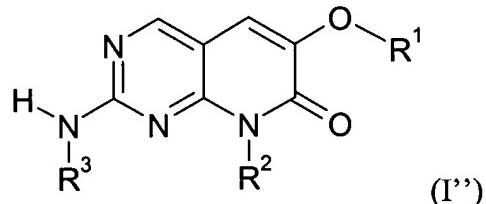
10 6. The compound of Claim 5, or a pharmaceutically-acceptable salt thereof, wherein R³ is optionally-substituted heterocyclyl.

7. The compound of Claim 5, or a pharmaceutically-acceptable salt thereof, wherein R³ is hydroxyalkyl or alkoxyalkyl.

15 8. The compound of Claim 1, or a pharmaceutically-acceptable salt thereof, wherein R² is hydrogen, alkyl, aryl, cycloalkyl or heteroalkyl.

9. The compound of Claim 8, or a pharmaceutically-acceptable salt thereof, wherein R² is alkyl or hydroxyalkyl.

20 10. A compound according to Claim 1, having the Formula (I''),



wherein,

R¹ is alkyl;

25 R² is selected from hydrogen, alkyl, aryl, cycloalkyl and heteroalkyl; and

R³ is heteroalkyl or heterocyclyl, or a pharmaceutically-acceptable salt thereof.

11. The compound of Claim 10, or a pharmaceutically-acceptable salt thereof, wherein R³ is selected from (1-hydroxy-2-methyl)-prop-2-yl, 1-hydroxy-pentan-2-yl, (S)-2-hydroxy-1,2-dimethyl-propyl, (R)-2-hydroxy-1,2-dimethyl-propyl, (S)-2-hydroxy-1-methyl-ethyl, 1-hydroxymethyl-cyclopentan-1-yl, 2-hydroxy-2-methyl-propyl, 3-methoxy-1(2-methoxy-ethyl)propyl, tetrahydro-2H-pyran-4-yl, 1-(methylsulfonyl)piperidin-4-yl, 1-carboxyethyl)piperidin-4-yl, 1,1-dioxidotetrahydro-2H-thiopyran-4-yl, and morpholinyl.

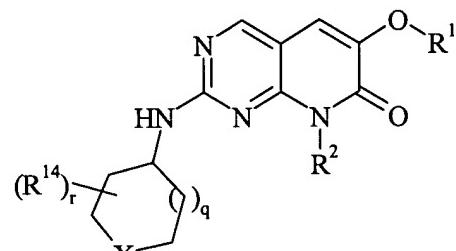
12. The compound of Claim 10, or a pharmaceutically-acceptable salt thereof, wherein:

10 R¹ is ethyl;

R² is methyl; and

R³ is selected from (1-hydroxy-2-methyl)-prop-2-yl, 1-hydroxy-pentan-2-yl, (S)-2-hydroxy-1,2-dimethyl-propyl, (R)-2-hydroxy-1,2-dimethyl-propyl, (S)-2-hydroxy-1-methyl-ethyl, 1-hydroxymethyl-cyclopentan-1-yl, 2-hydroxy-2-methyl-propyl, 3-methoxy-1(2-methoxy-ethyl)propyl, tetrahydro-2H-pyran-4-yl, 1-(methylsulfonyl)piperidin-4-yl, 1-carboxyethyl)piperidin-4-yl, 1,1-dioxidotetrahydro-2H-thiopyran-4-yl, and morpholinyl.

13. The compound of Claim 10, or an isomer, prodrug, or pharmaceutically-acceptable salt thereof, having the formula:



20

wherein:

X is -O-, -C(=O)-, -N(R^{12a})-, or -CH(R^{12b})-;

R^{12a} is selected from hydrogen, C₁₋₄alkyl, -C(=O)R¹⁵, -C(O)₂R¹⁵, and -S(O)₂(C₁₋₄alkyl);

R^{12b} is selected from hydrogen, C₁₋₄alkyl, -OR¹⁵, -C(=O)R¹⁵, -C(O)₂R¹⁵, and -S(O)₂(C₁₋

25 alkyl);

R^{14} is selected from $C_{1-4}alkyl$, oxo ($=O$), $-OR^{15}$, $-C(=O)R^{15}$, $-C(O)R^{15}$, and $-S(O)_2(C_{1-4}alkyl)$; and

R^{15} is at each occurrence independently selected from each other R^{15} from hydrogen and $C_{1-4}alkyl$;

5 q is 0 or 1; and

r is 0, 1 or 2.

14. The compound of claim 13, or an isomer, prodrug, or pharmaceutically-acceptable salt thereof, wherein X is $-N(R^{12a})-$, and R^{12a} is $-S(O)_2(C_{1-4}alkyl)$.

10

15. A pharmaceutical composition comprising:
a pharmaceutically acceptable excipient; and a compound of Claim 1 or a pharmaceutically acceptable salt thereof.

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16. A method for treating a p38 mediated disorder comprising administering to a patient in need of such treatment, an effective amount of a compound of Claim 1.

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17. The method of Claim 16, wherein said p38 mediated disorder is rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, Crohns disease, irritable bowel syndrome, inflammatory bowel disease, psoriasis, adult respiratory distress syndrome, asthma, or chronic obstructive pulmonary disease.

18. The method of Claim 16, wherein said p38 mediated disorder is Alzheimer's disease.

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